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Date : June 18, 2003

From : Robert L. Buchanan

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To : Examiner M.. Audet

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Direct :

Pages : 7

(including cover sheet)

If you received a partial delivery, please call _____ at _____.

Re: USN#09/551,336 by Holm et al.

Dear Examiner Audet: Here is the ISR material you requested. Please do not hesitate to call me at 617-517-5561 should you require any other documents from my file. I have asked the inventors to send me the Written Opinion and Form 409 that you requested. When I receive it, I will send it to you.

Regards,
R.L. Buchanan
Tel: 617-517-5561

INSIDE

Fax

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Received from <617 439 4170> at 6/18/03 2:11:19 PM [Eastern Daylight Time]

USSN 09/551,336 M. ADET

999899748

PCT COOPERATION TREATY

01.10.1998 PCT

REC'D 17 SEP 1998

WIPO

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P199600050 WO	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/DK97/00375	International filing date (day/month/year) 09.09.1997	Priority date (day/month/year) 09.09.1996
International Patent Classification (IPC) or national classification and IPC C 07 K 1/04		
Applicant Holm, Arne et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been enclosed and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 07.04.1998	Date of completion of this report 02.09.1998
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 3333 S-102 41 STOCKHOLM Facsimile No. 08-667 72 88 Form PCT/IPEA/409 (cover sheet) (January 1994)	Authorized officer Carolina Palmcrantz Telephone No. 08-782 25 00

USSN 09/551,336

M. Aude T

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/DK97/00375

I. Basis of the report

1. This report has been drawn on the basis of Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 19 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.

☒ the international application as originally filed.☐ the description, pages _____, as originally filed,

pages _____, filed with the demand,

pages _____, filed with the letter of _____,

pages _____, filed with the letter of _____.

☐ the claims. Nos. _____, as originally filed,

Nos. _____, as amended under Article 19,

Nos. _____, filed with the demand,

Nos. _____, filed with the letter of _____,

Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,

sheets/fig _____, filed with the demand

sheets/fig _____, filed with the letter of _____,

sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____☐ the claims. Nos. _____☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the supplemental Box (Rule 70.2(e)).

4. Additional observations, if necessary:

09/551,336 M. N. Let

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/DK97/00375

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-39	YES
	Claims		NO
Inventive step (IS)	Claims	1-39	YES
	Claims		NO
Industrial Applicability (IA)	Claims	1-39	YES
	Claims		NO

2. Citations and explanations

The present application pertains to a process and to an agent for the production of peptides by solid-phase synthesis (SPPS). The C-terminal part of the peptide which is attached to the solid support comprises a pre-sequence of 3 to 9 amino acid residues. The amino acid residues are selected from native L-amino acids having a side chain functionality which is protected during the coupling steps and having a propensity factor $P\alpha$ higher than 0.57 and a propensity factor $P\beta$ higher than 1.10 or the corresponding D-amino acids.

By incorporating a pre-sequence, having particular conformational parameters, at the C-terminus coupling times are reduced and incomplete peptide bond formation is avoided. Thus, by practising the method according to the present application 'difficult sequences' (sequences to which incomplete couplings are more prevalent) can be produced in high yield and purity.

The International Search Report revealed one document of interest:

A) US, A, 5021550

Document A discloses a method for preventing deletion sequences in solid phase synthesis of, e.g., polypeptides by providing an intermediate polypeptide covalently bound to a solid support. The intermediate polypeptide is then covalently bound to an amino acid moiety. Intermediate polypeptides which have successfully reacted with a further amino acid moiety remain bound to the solid support while unreacted intermediate polypeptides become covalently bound or otherwise attached to the solid support in at least two locations, i.e. they become 'cyclized'.

.../...

PCT/PEA/409 (Box V) (January 1994)

US5N 09/557,336

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/DK97/00375

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: V

Therefore, in view of document A it is not considered to be obvious to a person skilled in the art to solve the problem of incomplete peptide bond formation by using an intermediate polypeptide or pre-sequence of 3 to 9 amino acid residues and having a propensity factor $P\alpha$ higher than 0.57 and a propensity factor $P\beta$ higher than 1.10.

Thus, claims 1-39 are considered to fulfil the requirements of novelty, inventive step and industrial applicability.

USSN 09/557,336

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/DK 97/00375

3

A. CLASSIFICATION OF SUBJECT MATTER

IPC6: C07K 1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC6: C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI, CA, US PATENTS FULLTEXT, MEDLINE, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5021550 A (ALLEN R. ZEIGER), 4 June 1991 (04.06.91)	1-39

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

* Special categories of cited documents

"A" document disclosing the general state of the art which is not considered to be of particular relevance

"B" earlier document not published on or after the international filing date

"I" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, etc. exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, each contributing being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

12 November 1997

Date of mailing of the international search report

01-12-1997

Name and mailing address of the ISA/

Swedish Patent Office

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Authorized officer

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Form PCT/ISA/210 (second sheet) (July 1992)

USSN 09/557,336

M. P. Let

INTERNATIONAL SEARCH REPORT

Information on patent family members

01/10/97

International application No.

PCT/DK 97/00375

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5021550 A	04/06/91	US 5310894 A	10/05/94

Form PCT/ISA/210 (patent family annex) (July 1992)